Australian Government
Department of Health
Therapeutic Goods Administration

COVID-19 rapid antigen self-tests

Guidance on performance requirements and risk mitigation strategies

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TGA Health Safety Regulation

Contents

Purpose

The purpose of this document is to provide manufacturers and sponsors with guidance on the Therapeutic Goods Administration's (TGA) requirements concerning performance requirements (e.g. analytical and clinical sensitivity and specificity) and risk mitigation for COVID-19 rapid antigen self-tests.

This guidance refers to COVID-19 (caused by SARS-CoV-2) only and does not include self-tests to detect other types of coronavirus, or COVID-19 rapid antibody tests. COVID-19 rapid antigen self-tests are tests that allow individuals to collect a specimen, conduct a test and interpret the results by themselves. These tests can be performed in the home, without the involvement of a health professional. COVID-19 rapid antigen tests are most accurate when used in a symptomatic person within the first few days of showing symptoms (i.e. when the viral load is highest), although their accuracy has been shown to be lower than that of polymerase chain reaction (PCR) tests.

This document identifies key risks that must be mitigated and identifies conditions that may be imposed on the supply of self-test kits if they are to be included in the ARTG. Additional mitigation strategies, including conditions of inclusion may apply to individual devices on a case-by-case basis.

For further information on overall technical documentation requirements for in vitro diagnostics, please refer to the clinical evidence guidelines supplement: In vitro diagnostic (IVD) medical devices, guidance on the application audit (technical file review) of IVD medical device applications and guidance on the classification of IVD medical devices.

Please note:

The analytical and clinical performance requirements assigned to rapid antigen self-tests in this guidance are considered state of the art for COVID-19 rapid antigen tests. As these are the same category of rapid antigen tests used at the point-of-care (POC), these particular technical requirements are also considered applicable to rapid antigen point-of-care tests (POCT). The usability studies are specific to rapid antigen self-tests. This guidance is being published to allow sponsors and manufacturers to prepare their documentation for a COVID-19 rapid antigen test.

Background

Therapeutic Goods Act 1989 (the Act) requires that quality, safety and performance characteristics of medical devices be balanced with timely availability, and provides a system of controls for the regulation of therapeutic goods in Australia. Home-use tests (also known as self-tests) are therapeutic goods.

On 4 September 2020, after public consultation and following a review of self-testing regulations, the *Therapeutic Goods (Medical Devices – Excluded Purposes) Specification 2020* (the Excluded Purposes Specification 2020) was made, and came into effect on 1 October 2020. This allowed sponsors and manufacturers to apply to the TGA to include certain types of IVD self-tests in the ARTG.

However, COVID-19 rapid antigen self-tests remained prohibited and could not be supplied in Australia, under the Excluded Purposes Specification 2020. Therefore, before applications for these types of self-tests could be submitted, the Excluded Purposes Specification 2020 required

amendment to include self-tests for COVID-19. This occurred on 1 October 2021, with legal supply of the self-tests allowed from 1 November 2021.

Public health context

Following amendment of the Excluded Purposes Specification 2020, sponsors can apply for inclusion of COVID-19 rapid antigen self-tests in the ARTG. Each application is required to undergo evaluation by the TGA to ensure appropriate clinical performance requirements are met and risk mitigations are in place.

The European Centre for Disease Prevention and Control has published Public health implications of the use of self-tests to detect SARS-CoV-2 in the EU/EEA (europa.eu). This document highlights issues for consideration when approving COVID 19 tests for self-testing such as:

- the impact of disease prevalence on test results
- the impact of viral load and self-swabbing on test results, and
- frequency of self-testing on accuracy of results.

From a public health perspective, self-tests can offer advantages when used to complement existing PCR laboratory tests. They improve the accessibility to testing and allow individuals to obtain quick results, which could support the early detection of infectious cases and reduce further community transmission.

However, the introduction of self-testing could also lead to under-reporting of positive cases or it could lead to positive cases not being reported formally into state and territory public health systems. This can impact public health measures such as contract tracing, reporting of testing rates, reporting of case numbers, and epidemiological monitoring of variants of concern. Apart from viral load, the reliability of COVID-19 rapid antigen test results is also dependent on the successful collection of a suitable sample and appropriate timing for conducting a test, in relation to the onset of an individual's symptoms.

Consideration also needs to be given to the possibility that relatively high COVID-19 rates are required in a population before rapid antigen test results are reliable. The March 2021 Cochrane systematic review assessing rapid antigen tests for the detection of SARS-CoV-2 infection (COVID-19) suggested that at 0.5% prevalence asymptomatic screening would result in 70-90% of rapid antigen tests being false positives and 30-50% of cases being missed.

For successful implementation of self-testing in Australia, these risks need to be appropriately managed and mitigated to the extent possible. Different state and territory jurisdictions may have differing testing and reporting requirements based on their public health orders. The responsibility for reporting positive test results to state and territory health departments typically rests with the individual being tested.

Serology tests for the detection of antibodies to SARS-CoV-2 virus are not suitable for the diagnosis of COVID-19 and provide retrospective information only.

Performance characteristics and risk mitigation strategies for self-tests

All self-tests for serious diseases should meet the highest possible standard of clinical performance, relative to the intended purpose and classification of the test (essential principles 14 and 15 of Schedule 1, *Therapeutic Good (Medical Devices) Regulations 2002*. This approach is to balance the need for high quality tests with clinical characteristics that are fit for purpose.

Manufacturers of COVID-19 rapid antigen self-tests must also demonstrate they meet the specific requirements for self-tests in accordance with essential principle 15:

- An IVD medical device must be designed and manufactured in a way in which the analytical and clinical characteristics support the intended use, based on appropriate scientific and technical methods.
- Analytical performance is defined as the ability of an IVD medical device to detect or measure a particular analyte. Whereas the clinical performance is defined as the ability of the device to yield results that are correlated with a particularly clinical condition/physiological state in accordance with target population and intended user.
- An IVD medical device must be designed in a way that addresses accuracy, precision, sensitivity, specificity, stability, control of known relevant interference and measurement of uncertainty, as appropriate.
- An IVD medical device for self-testing must be designed and manufactured so it performs appropriately for its intended purpose, taking into account the skills and the means available to users and the influence resulting from variation that can reasonably be anticipated in the user's technique and environment.
- The information and instructions provided by the manufacturer of an IVD medical device for self-testing must be easy for the user to understand and apply.
- An IVD medical device for self-testing must be designed and manufactured in a way that reduces, to the extent practicable, the risk of error in the use of the device, the handling of the sample and the interpretation of results.

Overall acceptability of any test for the purposes of inclusion in the ARTG depends on compliance of the test device with the essential principles and in particular, a demonstration that the test does not compromise health and safety, is suitable for the intended purpose and the benefits of the test outweigh any residual risks associated with its use (essential principles 1, 2, 3 and 6).

Requirements for COVID-19 rapid antigen self-tests

COVID-19 rapid antigen self-tests are intended to be used in the home or similar environment by a lay person. Individuals with positive results should be directed to check for any additional testing or reporting requirements with their relevant state or territory health department. A negative result does not mean a person does not have COVID-19. If a person has symptoms, they should follow the guidance from the local state or territory health departments, and if unwell seek medical assistance.

Instructions provided by the manufacturer for the collection of samples and how to perform the test should be well-designed, easy to read, locally adapted and user friendly. Instructions should clearly describe the environmental conditions, incubation times, time between sampling and

reading, and correct interpretation of positive and negative results, in an illustrated and accessible way so they can be easily followed by a lay person. The instructions need to be usable by individuals of different literacy levels and be available in multiple languages. Clear, detailed instructions with a step-wise process to follow can significantly reduce errors in the performance of a rapid self-test.

Please note:

For an IVD medical device for self-testing, a lay person is defined as an individual who does not have formal training in a medical field or discipline to which the self-testing relates.

For the full definition, refer to the *Therapeutic Goods (Medical Devices) Regulations 2002*.

Analytical requirements

The evidence required to demonstrate the analytical performance characteristics of the test must be provided. When submitting an application for inclusion in the ARTG, the technical file is expected to include analytical studies such as:

- **Sample stability** – studies as relevant to the instructions for self-collection and conducting the test. Studies should cover all sample types intended for use with the test for the claimed sample storage time and temperature range.
- **Analytical sensitivity** – studies to establish the limit of detection of the test and reflect test performance using different sample types, including information specific to saliva when it is claimed as a sample type (required for SARS-CoV-2 and all relevant variants of concern in global circulation).

  Note: the limit of detection is the smallest amount of viral antigen that can be reliably detected by the test. COVID-19 rapid antigen self-tests should have an analytical sensitivity of at least 10^2 - 10^3 $TCID_{50}$/mL[1] accompanied with a Ct value which states the number of copies of virus per mL. If using recombinant protein (for variants of interest) this should be stated in ng/mL, with translation to viral particles per mL.
- **Analytical specificity** – studies to demonstrate the test detects all SARS-CoV-2 strains and will not produce a false positive result due to cross-reactivity with other human coronavirus (except SARS-CoV-1) or interference by an unrelated pathogen or substance.

  Studies should include non-infected individuals, potentially interfering and cross-reactive samples, and other respiratory pathogens, including bacteria.
- **Precision** – studies that address potential variability within-lot, between-lot, within-day, between-day, within-site, between-site and between-user.
- **High dose hook effect** – study to address the potential for false negative results at high level concentration of target antigen present in the sample.
- **Stability studies** – including:

[1] Technical specifications for selection of essential in vitro diagnostics for SARS-CoV-2 (who.int)

- open and closed shelf-life studies for the kit (test strip, buffer) that consider the extremes of temperature and humidity the tests may be exposed to in Australia; and
- transport simulation studies relevant to the claimed shelf-life and environmental conditions for storage, transport and use (e.g. temperature and humidity).

Consideration may be given to the assignment of a nominal (reduced) shelf life based on accelerated stability studies, provided they have been conducted under exaggerated conditions that include elevated temperature, high humidity, increased light and vibration, as appropriate. Ongoing real time studies are required to be monitored closely.

- **Validation of internal control** (all self-tests must include an internal control for the user to verify correct performance of the test).

Evidence to support the analytical performance of a COVID-19 rapid antigen test is required for both self-tests and point-of-care tests.

Clinical characteristics and clinical performance requirements

Evidence to support the clinical performance of a COVID-19 rapid antigen test is required for both self-tests and point-of-care tests. Manufacturers need to clearly identify if their device is intended to detect COVID-19 in symptomatic individuals only or also in asymptomatic individuals.

Symptomatic testing

COVID-19 rapid antigen tests are expected to provide clinical sensitivity and specificity studies that demonstrate the performance of the test when used to test symptomatic individuals. The studies should also demonstrate the clinical sensitivity of the test to detect the predominant variants of concern and variants of interest in global circulation (e.g. Delta variant, Omicron variant). A clinical performance study which evaluates the device's performance using clearly characterised study participants and considers the range of variable factors associated with use of the device must be provided.

It is anticipated self-tests will predominantly require the use of nasal swabs, however some tests may also include use of alternative specimen types such as saliva. All claimed sample types, as stated in the intended purpose of the test, must undergo clinical evaluation. Manufacturers claiming their rapid antigen test identifies COVID-19 in nasal swabs or saliva must conduct parallel testing or analysis of paired samples, to demonstrate specimen equivalence with other sample types also used in the clinical validation studies (e.g. nasopharyngeal swabs). It is expected that sample stability will be demonstrated for all claimed specimen types intended for use with the test.

The TGA expects statistically appropriate specimen numbers and sample selection for the evaluation of a COVID-19 rapid antigen test. For example, the European Commission's Medical Device Coordination Group (MDCG 2021-21) provides guidance on the performance evaluation of SARS-CoV-2 IVDs, including for COVID-19 rapid antigen tests (POCT and self-test).

Positive samples included in a clinical study are expected to be fully characterised (e.g. description of patient symptoms; day of collection post symptom onset; RT-PCR crossing threshold (Ct) values) and discordant results investigated. Positive samples need to be collected across the full range of days post on-set of symptoms and the peak period for detection must be

consistent with the claims made for the device. At least 20% of specimens should have Ct values >30 on the comparator PCR assay.[2]

Contrived samples are not acceptable in determining clinical sensitivity and specificity.

As a minimum, COVID-19 rapid antigen tests must meet the following clinical performance requirements for sensitivity and specificity for each of the claimed specimen types:

- a clinical sensitivity of at least 80% (for specimens collected within 7 days of symptom onset)
- a clinical specificity of at least 98%.[3]

An analysis of clinical sensitivity should focus on samples taken from patients at the peak time for viral shedding and viral load (i.e. within the first 7 days following onset of symptoms). Clinical information provided should include when samples were taken and tested (i.e. days post symptom onset) and clearly demonstrate the optimal days for testing.

Asymptomatic screening

Manufacturers that want to include claims relating to the detection of COVID-19 in asymptomatic individuals will need to provide evidence to support this.

The use of COVID-19 rapid antigen tests to test asymptomatic individuals for SARS-CoV-2 is generally associated with markedly reduced clinical performance, when compared with testing individuals who display typical signs or symptoms associated with COVID-19. In community settings that have low prevalence of COVID-19 (<0.5%), there is also an increased likelihood of false negative and false positive results produced by COVID-19 rapid antigen tests, which further reduces the reliability of results.

A March 2021 Cochrane review[4] found rapid antigen test sensitivity in asymptomatic patients ranged from 40.2-74.1%. A Norwegian study[5] compared a rapid antigen tests to PCR in 4857 parallel samples, finding the sensitivity of 55.3% in asymptomatic persons increased to 83.8% in the subset with high viral load. This suggests that better identification of COVID-19 occurs in more infectious individuals.

Notwithstanding the lower accuracy of rapid antigen testing there are some circumstances where testing of asymptomatic individuals may provide benefit. For example, preventing disease spread by testing close contacts of individuals known or suspected of being infected with COVID-19, or identifying individuals in the pre-symptomatic phase of COVID-19. Repeated, or serial testing (i.e. 2-3 times per week) is also thought to increase the detection rate of COVID 19 in some individuals before they exhibit symptoms.

Where manufacturers opt to include claims relating to testing of asymptomatic individuals in their COVID-19 test plan, performance of the test when used in this sub-population is required to be demonstrated, and clinical data separately presented in the instructions for use (IFU). This will allow users performing a test to understand that the reliability of their results is expected to be reduced if they do not have symptoms of COVID-19.

For studies to demonstrate performance in asymptomatic individuals, it is recommended testing should be performed on a minimum of 20 consecutively collected asymptomatic positive specimens and at least 100 consecutively collected negative specimens. All specimens should

[2] WHO Prequalification criteria for Emergency Use Listing (EUL) submission
[3] mdcg_2021-21_en.pdf (europa.eu)
[4] Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection - Dinnes, J - 2021 | Cochrane Library
[5] Diagnostic performance of a SARS-CoV-2 rapid antigen test in a large, Norwegian cohort (nih.gov)

also be tested with a comparator PCR test.[6] Discrepant analysis should be undertaken for all discordant results.

Usability studies

As self-tests will predominantly be used by lay persons, clinical evidence in the form of usability studies is required to establish performance of the test in the hands of these users. It is expected the clinical performance studies would include clinical patient samples in their usability studies. Specific usability studies are not required for rapid antigen tests only intended to be used by a health professional at the point-of-care.

The manufacturer is not required to provide Australian-specific usability studies, but it is expected that studies will reflect the performance of the test in a comparable setting and relevant to the Australian population.

For a usability study, the study population should represent all ages of individuals intended to be able to use the test. Participants should represent varying education levels and ages and include individuals who may not use English as their preferred language. Participants with prior medical or laboratory training should be excluded. Participants who have prior experience with self-collection or self-testing for COVID-19 should also be excluded.

Testing should include a minimum of 100 participants to examine each of the following usability characteristics and take place in an actual use environment or simulated environment with supervision but not intervention by the supervisor/observer. The entire workflow should be performed by each individual participant doing the test, including sample collection, testing and results interpretation without assistance, influence, or guidance from the study observers.

Usability and user comprehension

Usability and user comprehension studies should take into account the ability of the user to interpret the IFU, and to ensure the labelling is clear and easy to follow (e.g. a questionnaire to assess the ability of users to correctly comprehend instructions for use, limitations, diagrams, result interpretation and access to follow-up services).

The participants should be observed (either in person or by remote visual monitoring, such as a video conference) during sample collection and performance of the test and all difficulties noted.

Usability studies should also include the interpretation of contrived results under supervision:

- To evaluate the ease of interpretation of results by a lay-user, contrived tests results are to be read and interpreted by a minimum of 100 lay-users.
- The contrived test results should reflect a range of results including non-reactive, reactive, weak reactive and invalid, with a higher proportion of the samples in the weak-positive range close to the cut-off or limit of detection of the test.
- Determination of concordance against reading and interpretation of the same test by professional or trained users for the test.
- Standards such as *IEC 62366-1 Application of Usability Engineering to Medical Devices* may provide further guidance and considerations and how to document such usability studies.

[6] It is expected that the comparator PCR test has regulatory approval, either in Australia or from a comparable overseas regulator.

Confirmation of sensitivity and specificity in the hands of lay persons

The usability studies should confirm the diagnostic sensitivity and specificity of the test in hands of a lay person in the self-testing environment. The diagnostic sensitivity and specificity in the hands of the lay person should be estimated in comparison with the results of the professional test, i.e. by RT-PCR testing.[7]

- Diagnostic sensitivity, non-supervised – at least 30 lay users that are known antigen positive.
- Diagnostic specificity, non-supervised – at least 60 lay users that do not know their status.

The suitability of these studies will be assessed on a case-by-case basis and will depend on how well the manufacturer has mitigated any risks and demonstrated the overall benefits of the product outweigh any residual risks associated with its use. Demonstration of the benefit of a test and effectiveness of risk mitigation measures in the self-testing environment may be supported by a documented review of relevant published literature.[8]

Inter-reader variability

Inter-reader variability studies should consider the ability of at least 100 individuals to interpret pre-determined and/or contrived results. The samples need to consist of strongly positive results, a high proportion of weakly positive results, negative and invalid results to fully assess the ability of the lay person to obtain the correct result.

If the test uses an app to analyse or assist in the interpretation of results this needs to be used in the study to demonstrate there is no negative impact on interpretation, particularly for weak positive results.

A significant inter-reader variability (e.g. ≥ 5%[9]) for clearly positive or negative results implies the device is not easy to use, the IFU is not clear enough, or the test may be difficult to interpret resulting in an increased rate of false negative or false positive results.

Invalid test rate

The incidence of operational errors and test system failures (e.g. failure to sample correctly or complete each of the sequential steps required to perform the test, resulting in an invalid or unreadable result), or where the user is unable to interpret the result leading to an invalid result, should be determined. Physical completion of all the steps required to complete the test, by at least 60 individuals will provide an indication of the reliability and robustness of the test. Ideally the invalid test rate would be expected to be ≤ 5%[10] of the total tested (this includes defective tests or components).

[7] EU Specifications - MDCG 2021-21 Performance evaluation of SARS-CoV-2 IVDs https://ec.europa.eu/health/sites/default/files/md_sector/docs/mdcg_2021-21_en.pdf

[8] The literature review may include data for devices used for similar intended purposes as the device under assessment.

[9] WHO - https://www.who.int/publications/m/item/technical-specifications-for-selection-of-essential-in-vitro-diagnostics-for-sars-cov-2

[10] WHO - https://www.who.int/publications/m/item/technical-specifications-for-selection-of-essential-in-vitro-diagnostics-for-sars-cov-2

Risks

When using COVID-19 rapid antigen tests, false negative results are more likely to occur if a test is performed outside the window of highest viral shedding of the SARS-CoV-2 virus. Highest viral shedding has been observed at the time of symptom onset to day 5 of illness.[11] A COVID-19 rapid antigen test has a lower level of sensitivity if testing is performed outside of this period. Rapid antigen tests may have different specifications for different specimen types (nasal, throat swab, saliva) and the quality of the specimen collected may also affect results.

False positive results are more likely to occur when COVID-19 prevalence in the community is low (i.e. <0.5%). Even though the negative predictive value (NPV) of the test is high, false negatives may occur even in high prevalence settings.[12] The Cochrane review suggested that at 0.5% prevalence, asymptomatic screening would result in 70-90% of rapid tests being false positives and 30-50% of cases being missed.[13] Hence, clinical utility will change as case numbers change.

The above risks are exacerbated in a self-testing environment due to individual user variability in the correct performance and interpretation of the test and adequate specimen collection (i.e. the risks are predominantly user focussed).

Risk mitigation strategies for self-tests

The proposed risk-mitigation strategies recognise that self-tests differ from laboratory-based tests and point-of-care tests in that the user is responsible for all aspects of the testing process from sample collection to test interpretation and reporting.

COVID-19 rapid antigen self-tests will be subject to mandatory application audits prior to entry in the ARTG. Application audits are conducted to verify devices submitted for inclusion in the ARTG meet the relevant legislative requirements. The *Therapeutic Goods (Medical Devices) Regulations 2002* specifies that IVD medical devices for self-testing are subject to mandatory auditing. Information on the requirements for mandatory auditing can be found at auditing of medical devices, including IVD medical devices.

Some of the mitigating strategies for COVID-19 rapid antigen self-tests are:

- The specimen collection process must be straightforward, the instructions for specimen collection must be clear and easy to understand, and the specimen able to be collected safely in the home testing environment. Without clear instructions, individuals may not collect an adequate sample for testing, which may decrease the accuracy of the test.
- The test must be easy to perform with minimal operator intervention or procedural steps. Extensive usability studies would be expected (e.g. device interpretation study, label comprehension study and observed self-testing studies).
- Access to additional resources or information to assist in the completion of the test e.g. online video for sample collection and test interpretation or simple graphical instructions in the correct use and performance of the device.
- The stability of the product should be demonstrated across a range of operational and environmental conditions expected to be encountered geographically within Australia.

[11] The Lancet – SARS-CoV-2, SARS-CoV and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic Muge Cevik

[12] Considerations on the use of self-tests for COVID-19 in the EU/EEA – EDC Technical Report

[13] Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection - Dinnes, J - 2021 | Cochrane Library

- The tests should be able to detect the predominant strains or variants of SARS-CoV-2 virus that are circulating globally (i.e. not just those currently prevalent within Australia).
- The public health implications of a false negative need to be considered and instructions for use must include the requirement that even with a negative test if symptoms are developed the individual must have a laboratory PCR test performed.
- A sponsor telephone helpline or on-line operators to be available to provide support. The operators must have been trained in the performance and interpretation of the self-test and be able to provide advice on where to access state and territory health authority information to check if further testing or reporting of positive results is required.

Requirements for the instructions for use (IFU)

The manufacturer/sponsor of a COVID-19 rapid antigen self-test is also required to clearly outline the limitations of the test and provide clear advice, in the IFU and/or other information provided with the test, including the following:

- clear and simple instructions on how to perform and interpret the test (this may involve images or visual representation of the instructions, flow diagrams or QR codes linking to online demonstrations or a video for performing the test).
- available in print, with online option in multiple languages (e.g. including local languages).
- information on what variants of COVID-19 the test can detect including information of any change in performance due to specific variants.
- the clinical sensitivity and specificity of the test (i.e. in a self-testing environment) must be clearly identified (including information on the clinical sensitivity/specificity of the test at various time points post symptom onset).
- clear information on when testing should be performed, based on clinical performance study results (e.g. test within the first 7 days of symptom onset when viral shedding/viral load is highest).
- clear warnings on the risk of false negative results, particularly if testing is not performed within the first 7 days of symptom onset.
- clear warnings that the tests are less reliable in the later phase of infection and in asymptomatic individuals.
- recommend repeat testing (e.g. within 1-3 days) if ongoing suspicion of infection, high risk setting or occupational or other requirement.
- negative results may not mean a person is not infectious and if symptoms are present the person must seek immediate further testing.
- a negative result does not rule out infection with another type of respiratory virus.
- information on other limitations of the test such as a positive result cannot necessarily determine whether a person is infectious.
- a statement to the user that the test can only be used once.
- warnings about the need for supervision in children.
- information on how to safely dispose of the kit and its contents.

- information on what to do if a positive result is received and the need for individuals to check local State or Territory requirements for reporting positive results.
- how to contact locally available support services including phone lines and websites.
- how to contact the TGA to report poor performance or usability issues in the self-test environment (report an issue via the Users Medical Device Incident Report, email iris@tga.gov.au or call 1800 809 361).

Associated software and mobile applications

Any associated software or mobile applications (such as a tool to read or interpret the results of a test on a mobile phone) need to be simple and easy to use, with any risk of misuse reduced as far as possible. If your app is a simple tool for recording and transmitting patient results or generating a digital record, then it would not be considered a medical device. If it analyses the results or enables interpretation of the test result it will be a medical device. Australian privacy and data protection laws (the *Privacy Act 1988*) would still apply.

If the app is designed to analyse the test result it will be considered as separate analysis IVD medical device software and require separate inclusion in the ARTG. This applies regardless of the technology platform used, including cloud components – this document uses the term "app" solely for ease of reading. You will be required to provide:

- minimum specifications for the device (e.g. smartphone) you intend your app to operate on (e.g. memory, processor capability, minimum operating system requirements, browsers, smartphone models, etc.).
- evidence to validate the performance of the app with the self-test, including usability, functional and non-functional performance. This evidence must show how the specificity, sensitivity and other performance criteria of the self-test is maintained when using the app, i.e. there should be no gap in accuracy when comparing the test alone to the test plus the app. The validation evidence should clearly set out all use cases/scenarios tested.
- data used for validation, including testing, training and generalisability where applicable.
- details of architecture and design of the app and associated hardware platforms, including cloud if applicable.
- evidence cybersecurity risks have been addressed and how data privacy has been managed as it relates to patient safety and Australian privacy and data protection law.
- clear instructions for lay people on how to use the app, as part of the IFU.

Post-market monitoring and standard conditions of inclusion

All sponsors of self-tests included in the ARTG have ongoing responsibilities under the Act, the Medical Device Regulations and the *Therapeutic Goods (Therapeutic Goods Advertising Code) Instrument 2021* (the Advertising Code), including conditions that apply automatically to all ARTG entries. These conditions facilitate post-market monitoring and include, but are not limited to, the following:

- allowing entry and inspections of premises
- delivery of device samples upon request
- availability of information, such as facilitating access to technical documentation that demonstrates compliance with the essential principles
- ensuring any advertising material relating to the medical device complies with regulatory requirements
- reporting details of certain incidents and performance issues to the TGA, and any overseas regulatory actions to the TGA if the product involved is from the same batch or production run that was supplied in Australia.

All sponsors are also required to report adverse events to the TGA.

Additional conditions may be applied

Depending on the performance of the test, the information provided in the IFU and robustness of the test, the TGA may impose additional non-standard conditions to mitigate any residual risk identified relating to the effective and safe use of the product or to facilitate the monitoring of potential trends.

These are likely to include a requirement that the sponsor:

- provide additional support for users of the test through provision of information that will direct users to on-line support services that consists of either a helpline or on-line interactive support service.
- provide on their web-site instructional videos or on-line simple graphical instructions in the correct use and performance of the device.
- provide to the TGA an electronic copy of the IFU to be displayed on the TGA website. Upon release of a new version of the IFU by the manufacturer, the sponsor must provide this to the TGA, within 3 busines days for display on the TGA website.
- submits to the TGA through the medical device Incident Reporting and Investigation Scheme (IRIS) all complaints (including adverse events) related to the use of performance of the device, as soon as they are received by the sponsor, for the next five (5) financial years. This includes but is not limited to adverse events and reports of false positive and false negative results.
- provide the TGA with regular post market surveillance reports for each reporting period commencing on the date of inclusion of the device in the ARTG and ending at the end of each month until 30 June 2022. Until 30 June 2022, reporting periods are on the final day of each month, with the report to be submitted no later than the final day of the following month. Following July 1, 2022, and each twelve (12) months thereafter for the next three (3) financial years. Reports must be provided to the TGA before 1 October after each reporting period.

- include in the post market surveillance reports information on the distribution of the product, numbers of tests sold and numbers of any adverse events including reported false positive or false negative results and problems with poor performance of the test in Australia and worldwide.
- provide the post-market reports to the TGA at the following email address, postmarketdevices@health.gov.au.

Any further conditions would be applied on a case-by-case basis and would depend on the evaluation of an individual product, the overall benefits, and how well any risks have been mitigated.

The most up to date conditions for rapid antigen tests are published on the TGA website:

- Conditions specific to COVID-19 rapid antigen self-tests
- Conditions specific to COVID-19 rapid antigen point-of-care tests

Post-market review

The TGA can conduct a post-market review of certain kinds of devices included in the ARTG. ARTG entries for COVID-19 rapid antigen self-tests will be subject to a post-market review. Sponsors will be required to provide evidence of the performance of their device with respect to the variants of concern, as well as their risk management plans to ensure continued performance with the emergence of new variants. In addition, sponsors may be asked to provide test kits for independent laboratory evaluation of the clinical sensitivity and specificity to verify their performance.

Advertising requirements

Advertisements in the public domain for IVDs, including self-tests, are subject to the requirements of the Act, including the requirement to comply with the Advertising Code

The Advertising Code specifies the requirements for advertising therapeutic goods to consumers. Notably, the Advertising Code requires that advertising for therapeutic goods must:

- be accurate, balanced, and not misleading or likely to be misleading and that all information presented has been substantiated;
- be consistent with the intended purpose on the ARTG; and
- present the good in accordance with the directions/instructions for use.

Additionally, advertisements for therapeutic goods must not:

- contain any claim, statement, implication or representation that the goods are safe, their use cannot cause harm, that they have no side effects or that the goods are effective in all cases;
- exaggerate the efficacy or performance of the product or encourage inappropriate use;
- state or imply that the goods are approved or endorsed by a government authority (e.g. stating “TGA approved”);

- must not be likely to lead people to delay necessary medical attention; and
- must not be inconsistent with public health campaigns.

It is also important to be aware that representations in consumer advertising that refer to the detection of COVID-19, are 'restricted representations'. Under the Act, restricted representations must not be used in consumer advertising without prior approval or permission from the TGA. Notices of approved and permitted representations are published on the TGA website.

More information on complying with the Advertising Code https://www.tga.gov.au/complying-advertising-requirements and further general information on advertising is available via the advertising hub on the TGA website.

Enquiries about the legislative requirements for advertising therapeutic goods can be submitted online

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Therapeutic Goods Administration	10 September 2021
V2.0	Update to allow for self-testing. Update to analytical requirements and additional conditions that may be applied.	Therapeutic Goods Administration	28 September 2021
V2.1	Update to • reflect current advice regarding confirmatory testing and reporting requirements for COVID-19 rapid antigen test results due to the differing testing and reporting requirements of the State and Territory jurisdictions based on their public health orders. • reflect that the analytical and clinical performance requirements for COVID-19 rapid antigen self-tests are also considered applicable to rapid antigen point-of-care tests (as these are the same category of rapid antigen tests used at the point-of-care).	Therapeutic Goods Administration	31 January 2022
V2.2	Rebuilt document to fix formatting issues following PDF publication of V2.1.	Therapeutic Goods Administration	11 February 2022

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